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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/544,881	08/08/2005	Yoshinori Kyotani	275155US0PCT	7176

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EXAMINER	
HABTE, KAHSAY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 10/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/544,881	KYOTANI ET AL.	
	Examiner	Art Unit	
	Kahsay Habte	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,9,18 and 23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,8,9,18,26 and 27* is/are allowed.

6)☒ Claim(s) *23,24,28 and 29* is/are rejected.

7)☒ Claim(s) *25 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 8-9, 18 and 23-30 are pending in this application.

Response to Amendment

2. Applicant's amendment filed 09/12/2006 in response to the previous Office Action (05/12/2006) is acknowledged. Rejections of claims 1-23 under 35 U.S.C. § 112, second paragraph (items 12a-12f), under 35 U.S.C. 101 rejection (item 13), and an obviousness-type double patenting rejection (items 4-11) have been obviated. The enablement rejection of claim 23 (item 3) has been maintained.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-24 and 28-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of diseases causes by stimulation of interleukin-1β production selected from osteoporosis or ichorrhemia, does not reasonably provide enablement for the treatment of immune system, inflammatory disease or ischemic diseases in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. There has been recited a method of treating immune system diseases, inflammatory diseases, or ischemic diseases

caused by stimulation of interleukin-1β production, but the specification is not enabled for such a scope.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The scope of the claims is not adequately enabled solely based on the inhibitory activity against interleukin-1β production provided in the specification (see pages 310-311). First, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided.
The immune system is the body's defense against infectious organisms and other invaders. Through a series of steps called the **immune response**, the immune system attacks organisms and substances that invade our systems and cause disease. The immune system is made up of a network of cells, tissues, and organs that work together to protect the body.
The cells that are part of this defense system are white blood cells, or **leukocytes**. They come in two basic types, which combine to seek out and destroy the organisms or substances that cause disease.

Leukocytes are produced or stored in many locations throughout the body, including the thymus, spleen, and bone marrow. For this reason, they are called the **lymphoid** organs. There are also clumps of lymphoid tissue throughout the body, primarily in the form of lymph nodes that house the leukocytes.

The leukocytes circulate through the body between the organs and nodes by means of the **lymphatic vessels**. Leukocytes can also circulate through the blood vessels. In this way, the immune system works in a coordinated manner to monitor the body for substances that might cause problems.

There are two basic types of leukocytes:

The **phagocytes** are cells that chew up invading organisms.

The **lymphocytes** are cells that allow the body to remember and recognize previous invaders.

There are a number of different cells that are considered phagocytes. The most common type is the **neutrophil**. Neutrophils primarily fight bacteria.

There are two kinds of lymphocytes: the **B lymphocytes** and the **T lymphocytes**. Lymphocytes start out in the bone marrow and either stays there and matures into B cells, or they leave for the thymus gland, where they mature into T cells. B lymphocytes and T lymphocytes have separate jobs to do: B lymphocytes are like the body's military intelligence system, seeking out their targets and sending defenses to lock onto them. T cells are like the soldiers, destroying the invaders that the intelligence system has identified. Here's how it works.

A foreign substance that invades the body is called an **antigen**. When an antigen is detected, several types of cells work together to recognize and respond to it. These cells trigger the B lymphocytes to produce antibodies. Antibodies are specialized proteins that lock onto specific antigens. Antibodies and antigens fit together like a key and a lock.

Once the B lymphocytes have produced antibodies, these antibodies continue to exist in a person's body. That means if the same antigen is presented to the immune system again, the antibodies are already there to do their job. That's why if someone gets sick with a certain disease, like chickenpox, that person typically doesn't get sick from it again. This is also why we use immunizations to prevent getting certain diseases. The immunization introduces the body to the antigen in a way that doesn't make a person sick, but it does allow the body to produce antibodies that will then protect that person from future attack by the germ or substance that produces that particular disease.

Although antibodies can recognize an antigen and lock onto it, they are not capable of destroying it without help. That is the job of the T cells. The T cells are part of the system that destroys antigens that have been tagged by antibodies or cells that have been infected or somehow changed. (There are actually T cells that are called "killer cells"). T cells are also involved in helping signal other cells (like phagocytes) to do their jobs.

Antibodies can also neutralize toxins (poisonous or damaging substances) produced by different organisms. Lastly, antibodies can activate a group of proteins called

complement that are also part of the immune system. Complement assists in killing bacteria, viruses, or infected cells.

All of these specialized cells and parts of the immune system offer the body protection against disease. This protection is called immunity. Humans have three types of immunity - innate, adaptive, and passive.

Innate Immunity

Everyone is born with innate (or natural) immunity, a type of general protection that humans have. Many of the germs that affect other species don't harm us. For example, the viruses that cause leukemia in cats or distemper in dogs don't affect humans. Innate immunity also includes the external barriers of the body, like the skin and mucous membranes (like those that line the nose, throat, and gastrointestinal tract), which are our first line of defense in preventing diseases from entering the body. If this outer defensive wall is broken (like if you get a cut), the skin attempts to heal the break quickly and special immune cells on the skin attack invading germs.

Adaptive Immunity

We also have a second kind of protection called adaptive (or active) immunity. This type of immunity develops throughout our lives. Adaptive immunity involves the lymphocytes (as in the process described above) and develops as children and adults are exposed to diseases or immunized against diseases through vaccination.

Passive Immunity

Passive immunity is "borrowed" from another source and it lasts for a short time. For example, antibodies in a mother's breast milk provide an infant with temporary immunity

to diseases that the mother has been exposed to. This can help protect the infant against infection during the early years of childhood.

Everyone's immune system is different. Some people never seem to get infections, whereas others seem to be sick all the time. As a person gets older, he or she usually becomes immune to more germs as the immune system comes into contact with more and more of them. That's why adults and teens tend to get fewer colds than children - their bodies have learned to recognize and immediately attack many of the viruses that cause colds.

Disorders of the immune system can be broken down into four main categories:

immunodeficiency disorders (primary or acquired)

autoimmune disorders (in which the body's own immune system attacks its own tissue as foreign matter)

allergic disorders (in which the immune system overreacts in response to an antigen)

cancers of the immune system

Immunodeficiency Disorders

Immunodeficiencies occur when a part of the immune system is not present or is not working properly. Sometimes a person is born with an immunodeficiency - these are called primary immunodeficiencies. (Although primary immunodeficiencies are conditions that a person is born with, symptoms of the disorder sometimes may not show up until later in life.) Immunodeficiencies can also be acquired through infection or produced by drugs. These are sometimes called secondary immunodeficiencies.

Immunodeficiencies can affect B lymphocytes, T lymphocytes, or phagocytes. Some examples of primary immunodeficiencies that can affect kids and teens are:

IgA deficiency is the most common immunodeficiency disorder. IgA is an immunoglobulin that is found primarily in the saliva and other body fluids that help guard the entrances to the body. IgA deficiency is a disorder in which the body doesn't produce enough of the antibody IgA. People with IgA deficiency tend to have allergies or get more colds and other respiratory infections, but the condition is usually not severe.

Severe combined immunodeficiency (SCID) is also known as the "bubble boy disease" after a Texas boy with SCID who lived in a germ-free plastic bubble. SCID is a serious immune system disorder that occurs because of a lack of both B and T lymphocytes, which makes it almost impossible to fight infections.

DiGeorge syndrome (thymic dysplasia), a birth defect in which children are born without a thymus gland, is an example of a primary T-lymphocyte disease. The thymus gland is where T lymphocytes normally mature.

Chediak-Higashi syndrome and **chronic granulomatous disease** both involve the inability of the neutrophils to function normally as phagocytes.

Acquired immunodeficiencies usually develop after a person has a disease, although they can also be the result of malnutrition, burns, or other medical problems. Certain medicines also can cause problems with the functioning of the immune system. Some examples of secondary immunodeficiencies are:

HIV (human immunodeficiency virus) infection/AIDS (acquired immunodeficiency syndrome) is a disease that slowly and steadily destroys the immune system. It is caused by HIV, a virus which wipes out certain types of lymphocytes called T-helper cells. Without T-helper cells, the immune system is unable to defend the body against normally harmless organisms, which can cause life-threatening infections in people who have AIDS.

Immunodeficiencies caused by medications. There are several medicines that suppress the immune system. One of the drawbacks of chemotherapy treatment for cancer, for example, is that it not only attacks cancer cells, but other fast-growing, healthy cells, including those found in the bone marrow and other parts of the immune system. In addition, people with autoimmune disorders or who have had organ transplants may need to take immunosuppressant medications. These medicines can also reduce the immune system's ability to fight infections and can cause secondary immunodeficiency.

Autoimmune Disorders

In autoimmune disorders, the immune system mistakenly attacks the body's healthy organs and tissues as though they were foreign invaders. Some examples of autoimmune diseases:

Lupus is a chronic disease marked by muscle and joint pain and inflammation. The abnormal immune response may also involve attacks on the kidneys and other organs.

Juvenile rheumatoid arthritis is a disease in which the body's immune system acts as though certain body parts such as the joints of the knee, hand, and foot are foreign tissue and attacks them.

Scleroderma is a chronic autoimmune disease that can lead to inflammation and damage of the skin, joints, and internal organs.

Ankylosing spondylitis is a disease that involves inflammation of the spine and joints, causing stiffness and pain.

Juvenile dermatomyositis is a disorder marked by inflammation and damage of the skin and muscles.

Allergic Disorders

Allergic disorders occur when the immune system overreacts to exposure to antigens in the environment. The substances that provoke such attacks are called allergens. The immune response can cause symptoms such as swelling, watery eyes, and sneezing, and even a life-threatening reaction called anaphylaxis. Taking medications called antihistamines can relieve most symptoms. Some examples of allergic disorders:

Asthma, a respiratory disorder that can cause breathing problems, frequently involves an allergic response by the lungs. If the lungs are oversensitive to certain allergens (like pollen, molds, animal dander, or dust mites), it can trigger breathing tubes in the lungs to become narrowed, leading to reduced airflow and making it hard for a person to breathe.

Eczema is a scaly, itchy rash also known as atopic dermatitis. Although atopic dermatitis is not necessarily caused by an allergic reaction, it more often occurs in kids

and teens who have allergies, hay fever, or asthma or who have a family history of these conditions.

Allergies of several types can occur in kids and teens. Environmental allergies (to dust mites, for example), seasonal allergies (such as hay fever), drug allergies (reactions to specific medications or drugs), food allergies (such as to nuts), and allergies to toxins (bee stings, for example) are the common conditions people usually refer to as allergies.

Cancers of the Immune System

Cancer occurs when cells grow out of control. This can also happen with the cells of the immune system. Lymphoma involves the lymphoid tissues and is one of the more common childhood cancers. Leukemia, which involves abnormal overgrowth of leukocytes, is the most common childhood cancer. With current medications most cases of both types of cancer in kids and teens are curable.

Since the nature and origin of immune disorders vary one from the other as shown above, to this day the treatment of immune disorders in general is not possible.

In claims 24 and 29, the treatment of inflammatory diseases or the treatment of inflammation in general is claimed. Enablement for the scope of "inflammation" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process which can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction.

There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is

caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

Since the nature and origin of inflammatory diseases vary one from the other as shown above, to this day the treatment of inflammatory diseases in general is not possible.

Like wise, ischemic diseases are very broad in nature. Note that ischemia is defined as a disease of an organ (e.g. heart, brain, kidneys, foot, etc.) that is not getting adequate blood flow and lacks vital oxygen and nutrients. Ischemic stroke and ischemic heart disease are examples of ischemic diseases.Stroke represents one of the most intractable medical challenges. Stroke is estimated to cause about 15% of deaths, behind only heart disease and cancer. Even those who survive normally suffer from

persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy as so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, thus trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatment, such as antiarrhythmics and antithrombotics don't get at the cause of the stroke or the damage caused, but are mostly done to insure adequate cardiac functioning.

Effective acute drug treatment of the stroke itself has so far proved to be beyond the reach of medical science. Major efforts have certainly been pressed in the area of neuroprotective therapeutics. Those studied have included use of Ca antagonists such as Levemopamil and flunarizine, to suppress neuronal calcium influx; NMDA antagonists (both competitive, such as APV and CPP, and non-competitive such as chlorpromazine, ifenprodil and Mg salts) as well as AMPA and kainate antagonists to block post-ischemic receptor-operated calcium channels; attempts to block arachidonic acid cascade or elimination of its metabolic products with agents such as lipogenase inhibitors and thromboxane; use of free oxygen radical scavengers such as superoxide dismutase, alpha-tocopherol, or allopurinol to inhibit the lipid peroxidation that damages cell membranes, which may indirectly help prevent intracellular calcium overload; anti-edema agents such as corticosteroids; use of 5-HT_{1A} receptor agonists to suppress 5-HT concentrations in the hippocampal extracellular space; use of CRF receptor antagonists to inhibit excitotoxic brain damage; use of serotonin 1A agonists such as

ipsapirone, or adenosine modulators such as vinpocetine, to stimulate adenosine, which may act as a protective agent by hyperpolarizing the postsynaptic neuron; use of platelet aggregation inhibitors such as prostacycline and ticlopidine, and other approaches as well.

Despite this vast outpouring of research, the skill level in this art is sufficiently low relative to the difficulty of the task that obtaining a neuroprotective treatment of stroke was, as of the filing date, not yet possible. Hence, accomplishing such a goal involves more than routine experimentation. As evidence for this, there is cited Chalmers (TiPS Vol 17, pages 166-172 April 1996), which states flatly on page 170 that, "At present, there are no effective neuroprotective agents that can clinically ameliorate the effects of stroke in humans." For example, Pentoxifylline has been one of the most intensely studied, with dozens of studies published on its properties. It appears to have a wide variety of effects on leucocytes, erythrocytes, neutrophils, plasma fibrinogen levels. These result in a wide-ranging ability to increase blood flow, resulting in effectiveness in some vascular disorders, especially intermittent claudication. Research with different administration methods, or different subcategories of stroke may well result in the discovery of how to get this drug to work, but the slowness and difficulty of this research shows clearly that this involves undue, not routine experimentation. Applicants' compounds have been subjected to far less study.

The scope of pyridazinones claimed have a variety of diverse heteroaryl substituents on alkyls, alkenyls in R^1, R^2, R^3 and X-Z variables as well as all N-containing rings at

NR^2R^3. No examples of heteroaryl-substituted derivatives have been made much less tested. Note that piperazine derivative compounds 18, 21, 83, 143, 149, 189, 192, 213, etc. are the only examples shown for the scope of NR^2R^3 in the test. Test procedures and assays are provided in the specification at pages 310-311 only for 32 compounds and it is concluded that the representative compounds of formula (I) demonstrated positive inhibitory activity with IC_{50} ranging from 0.24 μM to 8.55 μM, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of the diverse disorders embraced the instant claims. The disorders encompassed by the instant claims (i.e. method of treating a diseases caused by stimulation of interleukin-1β production), some of which have been proven to be extremely difficult to treat. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that inhibiting the interleukin-1β production would result in only the

specific site of tissue; this kind of treatment can not translated to all the possible treatment of any disease in regards to their therapeutic effects.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the compounds and the inhibition of interleukin-1β production, one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds due to the unpredictability of the role of inhibiting the KSP kinesin i.e. whether promotion or inhibition would be beneficial for the treatment of the diseases.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Response to arguments

Applicant's argument filed 09/12/2006 has been fully considered but it is not persuasive.

Applicants indicate that pages 1-2 of the specification discusses the link between the increased production of interleukin-1β that induces the synthesis of enzyme which is considered to take part in inflammation and the treatment of diseases such as rheumatism, arthritis, etc. Applicants argue, "The present inventors previously reported in WO 99/44995 that high inhibitory activity against interleukin-1β production was observed on phenylpyridazine derivatives. Recently, certain phenylpyridazine derivatives having inhibitory activity against nterleukin-1β production have been reported (JP 7-69894A, WO 98/41511, WO 99/10331, WO 99/10332, WO 99/25696, WO 00/50408). These reported compounds, however, are different in chemical structure from the compounds of the present invention". The examiner disagrees with applicants. Because there is disclosure about in this specification at pages 1-2 in other printed publication does not mean the claims are enabled for the treatment of enablement for the treatment of immune system, inflammatory disease or ischemic diseases in general. Applicants in their own admission, indicate that the compounds of said printed publications are different from their compounds. Note that every case is judged on its own merit. The issue is whether applicants are enabled for the treatment of immune system, inflammatory disease or ischemic diseases in general and not

whether applicants have a descriptive support for the treatment of immune system, inflammatory disease or ischemic diseases.

Applicants have also provided 9 publications (Rossenwasser, Chang et al., Assuma et al, Romas et al., Wilson et al., Chernow, Li et al., Mollina et al, and Arend et al.) to support their arguments. The examiner carefully reviewed said publications, but none of the reference link directly the treatment of immune system, inflammatory disease or ischemic diseases with the inhibition of interleukin-1β production. Applicants argue, "Rossenwasser (*J Allergy Clin. Immunol.*, 102(3) Sept. 1998) generally explains that IL-1 is involved in the onset of such diseases as immune system disease, arthralgias, septic shock and colitis in view of its relation with inflammation (left column, page 345, also Table II and III". Note that according to page 345 (left column), IL-1 is implicated in the treatment of many diseases e.g. central nervous system disorders, blood vessels, cancerous and virus-infected cells, LPS-mediated septic shock, etc., but that does not mean that applicant are enabled for the treatment of immune system, inflammatory disease or ischemic diseases. The same is true with the other 8 publications. None of the references discloses the successful treatment of immune system, inflammatory disease or ischemic diseases by the inhibition of interleukin-1β production.

Allowable Subject Matter

4. Claims1, 8-9, 18 and 26-27 are allowed.

Objection

5. Claims 25 and 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

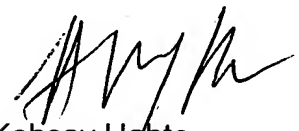
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kahsay Habte
Primary Examiner
Art Unit 1624

KH
October 23, 2006